ABSTRACT

A method for screening molecule which have a synthetic lethal property when in combination with a gene of interest carrying a non-lethal mutation, said method comprising the steps of: transfecting a first reporter gene into mammalian cells having a genome comprising a gene of interest which carries a non-lethal mutation, or a genome which is null of said gene of interest; selecting clones stably expressing said first reporter gene; introducing into said cells a survival plasmid comprising a functioning copy of said gene of interest, a second reporter gene, selectable marker, an origin of DNA replication and a nuclear antigen gene essential for replication of the plasmid within said cells, wherein said survivsal plasmid is autonomously replicating and spontaneously lost from said cells; growing said cells in the presence of a selection compound which selects for said selectable marker; selecting cell clones stably expressing said second reporter gene and said functioning copy of said gene of interest; removing selection for the selectable marker, and adding molecules destined for screening of their ability to impose selective pressure enforcing retention of the unstable survival plasmid. determining survival plasmid retention in cells, thus identifying a molecule having a synthetic lethal property when in combination with non lethal mutated gene of interest.